

## **REMARKS**

### **The Amendment of the Claims**

Claims 1-22 were canceled without prejudice by the amendment filed on November 2, 2005. Applicant reserves the right to prosecute the subject matter of any canceled claims in one or more continuation, continuation-in-part, or divisional applications. Claims 23 has been amended to incorporate the dose ranges of the active ingredient. The claim is supported by *e.g.*, claim 38 and paragraph [0122] of the specification originally filed. Claim 38 has been canceled. No new matter has been added. Claims 23-37 and 39-40 are pending in this application. Applicant respectfully submits that the pending claims are allowable for the following reasons.

### **The Claimed Invention is Not Obvious**

Claims 22-40 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over WO 02/064083 to Treston *et al.* (“Treston”) in view of U.S. Patent No. 6,479,512 to Fraley *et al.* (“Fraley”). (Pages 2-3 of the Office Action).

In particular, it is alleged that Treston teaches the use of S (-) 3-amino-thalidomide and R (+) 3-amino-thalidomide for the treatment of macular degeneration, dosages and pharmaceutical forms of the enantiomers, and that it would have been obvious to one skilled in the art to use the racemic mixture for the treatment. Page 3 of the Office Action. Applicant respectfully traverses the rejection.

Under the current law, prior art references cannot render a claim obvious unless the PTO provides evidence that the references meet a three-part test for *prima facie* obviousness. To begin with, the prior art reference or references must provide “motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant.” *See In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at \*4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at \*4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002).

Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, “[b]oth the suggestion and the reasonable expectation of success ‘must be founded in the prior art, not in the applicant’s disclosure.’” *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at 1515-16 (quoting *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996).

The pending claims recite, *inter alia*, methods of treating wet age-related macular degeneration comprising administering 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione in an amount of from about 0.1 mg to about 2 mg per day.

As the Examiner admits on page 3 of Office Action, Treston does not disclose or suggest the use of the specific compound recited in the claims in treating macular degeneration. Applicant points out that not only is that specific compound not taught nor is the specific disorder of the method claimed herein. Treston fails to teach or suggest the specific compound recited in the instant claims, less use for treating specific disease wet age-related macular degeneration as in the claimed methods or the use of the claimed dose. There must be a teaching or suggestion within the references to select the particular elements of the claimed invention. *Crown Operations International, Ltd. And Marshall H. Krone v. Solutia Inc.*, 289 F.3d 1367 (Fed. Cir. 2002). Thus, Treston does not provide one skilled in the art with any suggestion or motivation for the claimed methods.

It is alleged that Treston teaches the dosages of S (-) 3-amino-thalidomide and R (+) 3-amino-thalidomide on page 18, lines 10-19. (Office Action, page 3). As to the doses of the enantiomers, Treston discloses that 0.1 to 300 mg/kg/day, 0.5 to 50 mg/kg/day, and 0.1 to 2 mg/kg/day. *See* page 18, lines 15-18. However, the doses of about 0.1 to about 2 mg per day of the recited compound as claimed are not taught or suggested. Thus, Treston fails to suggest or motivate the methods using the specific amounts of the recited compound, and does not render obvious the instant claims reciting the specific amounts of a particular compound.

Further, nowhere does Treston teach or suggest that the particular disease, wet age-related macular degeneration, can be treated using the specific compound in specific amounts as recited in the present claims. Thus, from reading Treston, one skilled in the art would not have arrived at the claimed methods of treating patients with wet age-related macular degeneration with the recited compound in the specific amounts.

In sum, Treston is devoid of any teachings or suggestion on the use of the specific compound in specific methods, using the specific doses in a specific patient population against a specific disease. Treston fails to suggest or motivate the methods of using the specific amounts of the recited compound for treating a specific disease, and does not render obvious the instant claims. It has not been established that Treston teaches or suggests each and every limitations of the claimed invention herein.

**The Claimed Combination Therapies are Not Obvious**

It is alleged that Fraley discloses the use of a second active ingredient as angiogenesis inhibitors for the treatment of macular degeneration, and that the combination therapy is obvious to one skilled in the art. Page 3 of the Office Action. Applicant respectfully traverses the rejection.

Pending claims 30-33 recite, *inter alia*, methods of treating wet age-related macular degeneration comprising a second active agent and from about 0.1 mg to about 2 mg per day of the specific compound 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione.

As discussed above, a *prima facie* case of obviousness has not been established for the use of the specific compound 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione. Thus, the combination therapy using the compound and a second active agent cannot be obvious.

Fraley teaches that angiogenesis inhibitors can be used in combination with the compounds of the tyrosine kinase inhibitors disclosed therein. (Column 10, lines 21-35). However, Fraley is silent as to the specific compound 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione, let alone the specific amounts of from about 0.1 mg to about 2 mg per day, much less the use of the specific compound in specific amounts for treating wet age-related macular degeneration, as recited in the present claims. Thus, Fraley suggests nothing about the combination therapy using the recited compound and other agents in treating wet age-related macular degeneration as claimed. Accordingly, Treston in combination with Fraley does not provide any suggestion or motivation for the claimed methods using the recited compound in specific amounts and a second agent in treating wet age-related macular degeneration.

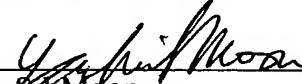
Thus, a *prima facie* case of obviousness has not been established and the rejection must be withdrawn.

**Conclusion**

In view of the foregoing, all the rejections of the claims should be withdrawn. Reconsideration, entry of the above amendment and remarks, and allowance of the pending claims are respectfully requested. Should the Examiner not agree that all claims are allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues and to accelerate the allowance of the above-identified application.

Respectfully submitted,

Date: April 25, 2007

  
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